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NOTICE OF ALLOWANCE AND FEE(S) DUE

22428 7590 10/09/2008

FOLEY AND LARDNER LLP
SUITE 500
3000 K STREET NW
WASHINGTON, DC 20007

EXAMINER	
MOORE, WILLIAM W	
ART UNIT	PAPER NUMBER
1656	

DATE MAILED: 10/09/2008

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/599,391	12/12/2006	Veakata Madhusudhan Reddy Mule	056859-0225	8017

TITLE OF INVENTION: RECOMBINANT CALF-CHYMOSIN AND A PROCESS FOR PRODUCING THE SAME

APPLN. TYPE	SMALL ENTITY	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	NO	$1510	$300	$0	$1810	01/09/2009

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the SMALL ENTITY status shown above.

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:

A. If the status is the same, pay the TOTAL FEE(S) DUE shown above.

B. If the status above is to be removed, check box 5b on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and twice the amount of the ISSUE FEE shown above, or

If the SMALL ENTITY is shown as NO:

A. Pay TOTAL FEE(S) DUE shown above, or

B. If applicant claimed SMALL ENTITY status before, or is now claiming SMALL ENTITY status, check box 5a on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and 1/2 the ISSUE FEE shown above.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

PTOL-85 (Rev. 08/07) Approved for use through 08/31/2010.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail **Mail Stop ISSUE FEE**
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INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

22428 7590 10/09/2008

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I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

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nonprovisional	NO	$1510	$300	$0	$1810	01/09/2009

EXAMINER	ART UNIT	CLASS-SUBCLASS
MOORE, WILLIAM W	1656	435-198000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

❑ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.

❑ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list

(1) the names of up to 3 registered patent attorneys or agents OR, alternatively,

(2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

1 _____

2 _____

3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE (B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent) : ❑ Individual ❑ Corporation or other private group entity ❑ Government

4a. The following fee(s) are submitted:

❑ Issue Fee

❑ Publication Fee (No small entity discount permitted)

❑ Advance Order - # of Copies _____

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❑ A check is enclosed.

❑ Payment by credit card. Form PTO-2038 is attached.

❑ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment, to Deposit Account Number _____ (enclose an extra copy of this form).

5. **Change in Entity Status** (from status indicated above)

❑ a. Applicant claims SMALL ENTITY status. See 37 CFR 1.27.

❑ b. Applicant is no longer claiming SMALL ENTITY status. See 37 CFR 1.27(g)(2).

NOTE: The Issue Fee and Publication Fee (if required) will not be accepted from anyone other than the applicant; a registered attorney or agent; or the assignee or other party in interest as shown by the records of the United States Patent and Trademark Office.

Authorized Signature _____ Date _____

Typed or printed name _____ Registration No. _____

This collection of information is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

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Determination of Patent Term Extension under 35 U.S.C. 154 (b)
(application filed after June 7, 1995 but prior to May 29, 2000)

The Patent Term Extension is 0 day(s). Any patent to issue from the above-identified application will include an indication of the 0 day extension on the front page.

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Extension is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (http://pair.uspto.gov).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

Notice of Allowability	Application No.	Applicant(s)	
	10/599,391	MULE ET AL.	
	Examiner	Art Unit	
	WILLIAM W. MOORE	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *amendments filed 27 September 2006 and the telephonic interview of 30 September 2008*.

2. ☒ The allowed claim(s) is/are *1-14*.

3. ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☒ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☒ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☒ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

/William W. Moore/ 30 September 2008	/ Nashaat T. Nashed, Ph.D. Supervisory Primary Examiner Art Unit 1652

EXAMINER'S AMENDMENT

Priority

Applicant's claim in the Declaration of Inventorship filed 12 December 2006 to priority of the 30 March 2004 filing date of the International patent application PCT/IN04/00074, is hereby acknowledged. Comparison of the amino acid sequence of SEQ ID NO:1 and the nucleic acid sequence of SEQ ID NO:2 set forth in the amended sheets 3 and 4, sequences required by claims 1-14 of amended sheets 15 and 16, shows however that these 27 September 2006-filed sequences differ from the amino acid and nucleic acid sequences set forth in the International application and published in WO 2005/094185. In particular,

(i) the new SEQ ID NO:1 depicts glycines at both position 146 and 147, asparagine at position 294, and tryptophan at position at position 342 whereas the chymosin amino acid sequence provided in the 30 March 2004-filed parent application depicts valines at positions 146 and 147, aspartate at position 294, and glycine at position 342, and

(ii) the nucleic acid sequence of the new SEQ ID NO:2 depicts the codons "GGA" and "GGC" at positions 436 through 441, the codon "AAC" at positions 880-882, and the codon "TGG" at positions 1024-1026, whereas the chymosin-encoding nucleic acid sequence provided in the 30 March 2004-filed parent application depicts the codons "GTA" and "GTC" at positions 436-441, the codon "GAC" at positions 880-882, and the codon "GGG" at positions 1024-1026.

Consequently, the subject matter described by the replacement claims 1-14 enjoys only the priority of the 27 September 2006 filing date of this application.

Claim Amendments

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Amend claims 1-14 thus:

1. (Amended) An isolated ~~A~~ recombinant calf-Chymosin protein having the amino acid sequence ~~as~~ set forth in SEQ ID NO:1.
2. (Amended) An isolated ~~A~~ recombinant calf-Chymosin gene comprising the nucleic acid sequence ~~as~~ set forth in SEQ |D NO:2.
3. (Amended) The recombinant calf-chymosin gene of ~~as claimed in~~ claim 2 consisting of the nucleic acid sequence of SEQ ID NO:2 encoding the ~~protein comprising~~ amino acid sequence of SEQ ID NO:1.

4. (Amended) An *E.coli* cell comprising the recombinant chymosin gene of SEQ ID NO:2.

5. (Amended) The E. *coli* of ~~as claimed in~~ claim 4 which is a BL21 cell *of E.coli.*

6. (Amended) An expression vector pET21b comprising the recombinant calf-chymosin gene as set forth in SEQ ID NO:2.

7. (Amended) A method for producing the recombinant calf-chymosin protein as set forth in SEQ ID NO:1 which comprises the steps of
(i) isolating a calf-chymosin gene encoding the calf-chymosin protein of SEQ ID NO:1,
(ii) cloning said gene ~~the same~~ in the bacterial expression vector pET2lb,
(iii) transforming said cloned vector into cells of *E.coli,*
(iv) fermenting said *E. coli* to produce pro-chymosin,
(v) converting said pro-chymosin to chymosin and
(vi) subsequently recovering the recombinant calf chymosin.

8. (Amended) The method of ~~as claimed in~~ claim 7, wherein the calf-chymosin gene is obtained by (i) isolating RNA from the fourth stomach of a calf ~~tissue,~~ and (ii) synthesizing ~~synthesising~~ a first strand of cDNA therefrom by treating the RNA ~~same~~ with a reverse primer of SEQ ID NO:3 and ~~then~~ with a forward primer of SEQ ID NO:4.

9. (Amended) The method of ~~as claimed in~~ claim 8, wherein the eDNA is ligated at the Sma**I** ~~sma1~~ site of the pBSSK+ plasmid and then transformed into TOP10 cells of *E. coli.*

10. (Amended) The method of ~~as claimed in~~ claim 9, wherein said recombinant clones were identified and treated with a forward primer of SEQ ID NO.5 and reverse primer of SEQ ID NO:6 containing Nde**I** and Hind**III** sites to obtain an amplified fragment.

11. (Amended) The method of ~~as claimed in~~ claim 10, wherein the amplified fragment is transformed into cells of *E.coli* for expressing the chymosin gene.

12. (Amended) The method of ~~as claimed in~~ claim 11, wherein *E.coli* cells containing recombinant calf-chymosin gene is fermented, the suspended cells produced on completion of fermentation are lysed, chilled and pH adjusted to about 8 before incubation at room temperature and the separation of supernatent containing prochymosin.

13. (Amended) The method of ~~as claimed in~~ claim 12, wherein
(i) the pH of the supernatant is adjusted to about pH 2 for activation,
(ii) the supernatant is further incubated for about 6 hrs, and
(iii) then subjected to filtration to obtain a filtrate.

14. (Amended) The method of ~~as claimed in~~ claim 13, wherein

(i) the filtrate is subjected to sodium chloride precipitation, ~~then~~

(ii) the resulting precipitate is dissolved and

(iii) ~~followed by the addition of~~ sodium benzoate is added as preservative.

Authorization for this examiner's amendment was given in a telephone interview with Ms. Qun Liu on 30 September 2008.

Reasons for Allowance

The following is an examiner's statement of reasons for allowance:

The examiner's amendment above clarifies the intended subject matter of claims 1-14 by ensuring that claim 3 has a lesser scope than claim 2 from which it depends, by correcting errors in grammar, by separating method steps in numbered clauses in claims 7, 13 and 14, and by simplifying the claims' recitations. The subject matter of claims 1-14 allowed herewith is free of the prior art made of record herein because there are three amino acid sequence differences relative to prior art prochymosins disclosed in Applicant's 30 March 2004 priority document and present as well in SEQ ID NO:1 as filed 27 September 2006. The first of these is the presence of serine at position 3 of SEQ ID NO:1 which was introduced by Applicant's use of the oligonucleotide primer of SEQ ID NO:5 herein. Glutamate, rather than the serine of SEQ ID NO:1 herein, is present at this position in the prior art teachings of Emtage et al. and Yonezawa et al., both made of record herewith who altered the amino-terminal amino acid sequence of chymosin for the direct expression of prochymosin in an *E. coli* host cell. Even the extensive modifications taught in Figure 1 and Table 2 of Yonezawa et al. all retain glutamate at the prochymosin position corresponding to position 3 of SEQ ID NO:1 herein.

Two other amino acid sequence differences disclosed in Applicant's 30 March 2004 priority document, and maintained in SEQ ID NO:1 as filed 27 September 2006, are the presence of aspartate at position 294 of SEQ ID NO:1 where an asparagine is invariably present at this position corresponding to position 309 in the naturally-occurring preprochymosin amino acid sequences, position 293 in the amino acid sequence of a prochymosin, and position 251 in the mature chymosins. Huang et al., among the prior art made of record herewith, teach a modification in the region of position 251 in the mature chymosin, making a C250D substitution at the adjacent cysteine, but are silent concerning any modification of the asparagine at position 251. The prior art also fails to teach or suggest that tryptophan occurs, or should be introduced, at a position corresponding to position 342 in the 27 September 2006-filed SEQ ID NO:1 herein; instead, a glycine occurs at the corresponding position 299 in mature chymosins of the prior art.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to William W. Moore whose telephone number is 571.272.0933 and whose FAX number is 571.273.0933. The examiner can normally be reached Monday through Friday between 9:00AM and 5:30PM EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisory Primary Examiner, Dr. Kathleen Kerr Bragdon, can be reached at 571.272.0931. The official FAX number for all communications for the organization where this application or proceeding is assigned is 571.273.8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571.272.1600.

/Nashaat T. Nashed/
Nashaat T. Nashed, Ph.D.
Supervisory Primary Examiner
Art Unit 1652

/William W. Moore/
30 September 2008